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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/716,739

11/18/2003

Murugan R. Pandian

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7590

05/18/2006

Donald E. Stout  
Stout, Uxa, Buyan & Mullins, LLP  
Suite 300  
4 Venture  
Irvine, CA 92618

EXAMINER

COUNTS, GARY W

ART UNIT

PAPER NUMBER

1641

DATE MAILED: 05/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/716,739	<b>Applicant(s)</b> PANDIAN ET AL.	
	<b>Examiner</b> Gary W. Counts	<b>Art Unit</b> 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 23 February 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 23,24 and 42-44 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 23,24 and 42-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### **Status of the claims**

Applicant's amendments filed February 23, 2006 is acknowledged and has been entered.

### **Rejections Withdrawn**

Applicant's amendment to claim 3 to delete the recitation "or" and insert "and" has overcome the 112 written description rejection.

Applicant's cancellation of claim 25 renders the 112 2<sup>nd</sup> rejection of claim 25 moot and therefore the rejection has been withdrawn.

### **Rejections Maintained**

#### ***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

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3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 23-24, 42 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al (Clinical Chemistry 47:2, 308-315, Feb. 2001) in view of O'Connor et al (US 6,500,627) in light of Birken et al (Immunochemical measurement of Early Pregnancy Isoforms of hCG: Potential Applications to Fertility Research, Prenatal Diagnosis, and Cancer, 32 (2001) 635-643) in view of Hochstrasser et al (US 2003/0157580) and Birken et al (US 6,521,416).

Cole et al disclose human chorionic gonadotropin immunoassays in the diagnosis of trophoblastic diseases. Cole et al disclose that patients with trophoblastic disease produce ordinary and irregular forms of human chorionic gonadotropin (p. 308). Cole et al disclose that trophoblastic disease include complete and partial hydatidiform mole, postmolar tumor, gestational choriocarcinoma, testicular choriocarcinoma, and placental site trophoblastic disease (p. 309). Cole et al discloses that patients can be diagnosed with choriocarcinoma solely from a persistent positive hCG result, in the

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absence of a pregnancy (p. 314). Cole et al is generic with respect to the reagents used in the immunoassay.

Cole et al differ from the instant invention in failing to specifically state the use of antibodies to the hyperglycosylated human chorionic gonadotropin and human chorionic gonadotropin and also fails to labels in the immunoassay in one assay.

O'Connor et al (US 6,500,627) disclose methods of detecting trophoblastic disease. O'Connor et al disclose that the trophoblastic disease can include choriocarcinoma or hydatidiform mole. O'Connor et al disclose contacting a sample from a subject with an antibody which specifically binds to a molecular isoform of hCG. O'Connor et al disclose contacting the sample with a second antibody which specifically binds to intact non-nicked hCG (hCG) (col 4 and col 25-26). O'Connor et al disclose B152 antibodies specific for the isoform of hCG (col 10, lines 40-44). Birken et al (Archives of Medical Research, 2001, 635-643) disclose that B152 is hyperglycosylated form (abstract). Therefore, O'Connor et al teaches detecting hyperglycosylated hCG. O'Connor et al disclose that the amount of B152 isoform (hyperglycosylated hCG) and hCG are increased in trophoblast disease (col 25-26 ). O'Connor et al also disclose that hCG is elevated in pregnancy. O'Connor et al discloses that the sample can be a blood or urine sample. O'Connor et al disclose that detection can be performed by using an labeled antibody. O'Connor et al disclose that the label can be a radioactive isotope such as I<sup>125</sup>.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate antibodies and labels as taught by O'connor et al

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into the method of diagnosing as taught by Cole et al because Cole et al specifically teaches that immunoassays are used for diagnosing trophoblastic disease and O'Connor et al teaches specific antibodies and labels used in immunoassays for diagnosing trophoblastic disease. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating antibodies and labels as taught by O'Connor et al into the method of Cole et al.

Cole et al and O'Connor et al fail to teach confirming the subject is not pregnant. Cole et al and O'Connor et al also differs from the instant invention in failing to teach comparing the determined amount of hyperglycosylated human chorionic gonadotropin present in the sample to sample obtained from subjects who do not have a trophoblastic disease and comparing the determined amount of human chorionic gonadotropin present in the sample to amounts obtained from subjects who do not have a trophoblastic disease.

Since Cole et al specifically teaches that non-pregnant subjects can be diagnosed with trophoblastic disease and also since the combination of Cole et al and O'Connor et al disclose that hyperglycosylated hCG and hCG are elevated in both trophoblastic disease and pregnancy one of ordinary skill in the art would consider that pregnancy would have to be excluded before determining trophoblastic disease and thus would confirm that the patient was not pregnant before determining trophoblastic disease. Further, Hochstrasser et al (abstract & page 1, paragraph 0012) teaches that in order to perform diagnostic assays on markers which are known to be involved in more than one condition, one must be able to distinguish between the two conditions

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and thus perform an assay to exclude one of the conditions. Therefore, it would have been obvious to one of ordinary skill in the art to confirm that the subject is not pregnant before detecting a trophoblastic disease.

Birken et al (US 6,521,416) discloses that analysis of the metabolites of gonadotropins in a sample can help to distinguish between healthy and abnormal physiological states. Birken et al (US 6,521,416) discloses thresholds to determine abnormal states (col 2, line 54 – col 3 , line 14). Birken et al disclose comparing the sample to normal subjects to determine the abnormal state.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate thresholds and samples from normal subjects as taught by Birken et al (US 6,521,416) into the modified method of Cole et al because Birken et al shows that this provides for the analysis of the metabolites of gonadotropins in a sample to distinguish between healthy and abnormal physiological states.

With respect to the a 50<sup>th</sup> percentile as recited in the instant claims, the optimum threshold in this case 50<sup>th</sup> percentile can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. “[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation.” Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). “No invention is involved in discovering optimum ranges of a process by routine experimentation .” Id. At 458,105 USPQ at 236-237. The “discovery of an optimum

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value of a result effective variable in a known process is ordinarily within the skill of the art.”

Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Also, one of ordinary skill in the art would optimize the assay to minimize the false positive and false negative results.

5. Claim 44 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cole et al (Clinical Chemistry 47:2, 308-315, Feb. 2001) and O’connor et al (US 6,500,627) in light of Birken et al (Immunochemical measurement of Early Pregnancy Isoforms of hCG: Potential Applications to Fertility Research, Prenatal Diagnosis, and Cancer, 32 (2001) 635-643) in view of Hochstrasser et al (US 2003/0157580) and Birken et al (US 6,521,416) as applied to claims 23-25, 42 and 43 above, and further in view of Campbell et al (US 4,946,958).

See above for teachings of Cole et al., O’Connor et al., Hochstrasser et al and Birken et al.

Cole et al., O’Connor et al., Hochstrasser et al and Birken et al differ from the instant invention in failing to teach the assay is a chemiluminescent sandwich assay.

Campbell et al disclose a chemiluminescent label which is conveniently linked to a monoclonal antibody or other protein and is used in immunoassay for the quantitation of an antigen of interest (abstract). Campbell et al disclose that the use of this chemiluminescent label in assays provides a means of improving the sensitivity of measurement of proteins and polypeptides by one to two orders of magnitude (col 7, lines 27).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the chemiluminescent label as taught by Campbell et al for the label of O'Connor et al because Campbell et al shows that the use of this chemiluminescent label in two-site assays provides a means of improving the sensitivity of measurement of proteins and polypeptides by one to two orders of magnitude.

***Response to Arguments***

6. Applicant's arguments filed 02/23/06 have been fully considered but they are not persuasive.

Applicant argues that one of ordinary skill in the art would not be motivated to combine the teachings of O'Connor and Cole. Particularly, Applicant states that a person of ordinary skill in the art would not be motivated to combine the teachings of O'Connor which discloses the use of monoclonal antibodies with the teachings of Cole directed to the use of broad spectrum antibodies, such as polyclonal antibodies. Applicant states that as understood by persons of ordinary skill in the art, monoclonal antibodies are highly specific and thus the use of monoclonal antibodies is contrary to the teachings of Cole which emphasize the importance of broad spectrum antibodies to detect hCG and all of its variants. This is not found persuasive because as stated by applicant and as known in the art. Monoclonal antibodies are more specific and thus would provide a higher specificity and reduce none specific binding. Further, Applicant's claims are directed to determining an amount of hCG and an amount of hyperglycosylated hCG and are not directed toward total hCG. Also, as stated in the previous office action the Examiner has relied upon Cole for teaching that it is known in

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the art to use immunoassays for the detection of trophoblastic disease and to also detect trophoblastic disease in non-pregnant patients and Examiner has relied upon O'Connor for teaching specific antibodies and reagents that are used for detecting trophoblastic disease. Also, it appears that the Applicant is arguing that Examiner has substituted the antibodies of O'Connor et al for the antibodies of Cole. This argument is not on point because the Examiner has not substituted the antibodies but has stated that it would have been obvious to one of ordinary skill in the art to incorporate antibodies as taught by O'Connor et al into the methods as taught by Cole. Further, it is noted that Applicant's claims contain open language (i.e. comprising) and therefore, the claims can include other components. Further, absent evidence to the contrary it appears that monoclonal antibodies would work in the methods of Cole et al. Therefore, as stated in the previous office action It would have been obvious to one of ordinary skill in the art to incorporate antibodies and labels as taught by O'Connor et al into the method of diagnosing as taught by Cole et al because Cole et al specifically teaches that immunoassays are used for diagnosing trophoblastic disease and O'Connor et al teaches specific antibodies and labels used in immunoassays for diagnosing trophoblastic disease. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating antibodies and labels as taught by O'Connor et al into the method of Cole et al.

### ***Conclusion***

7. No claims are allowed.

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8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

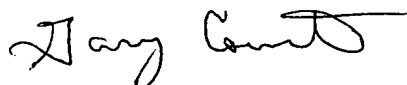
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gary Counts  
Examiner  
Art Unit 1641  
May 8, 2006



LONG V. LE  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600

05/12/06